



**U.S. FOOD & DRUG  
ADMINISTRATION**

CENTER FOR DRUG EVALUATION AND RESEARCH  
**OFFICE OF COMPLIANCE**  
**CALENDAR YEAR 2017**  
**ANNUAL REPORT**

Shielding patients from poor quality, unsafe and ineffective drugs through proactive compliance strategies and risk-based enforcement actions.

A close-up, low-angle photograph of a pharmaceutical manufacturing process. Several glass vials are being filled by a machine, with a bright light source creating a strong glow and lens flare effect. The vials are arranged in a row, and the machine components are visible in the foreground and background.

October 2018  
[www.fda.gov](http://www.fda.gov)

## CDER/Office of Compliance First-Ever Accomplishments

- Issued the first warning letter for a combination product that included drug and device violations of the Federal Food, Drug, and Cosmetic Act.
- Worked with the Department of Justice on the first consent decree for risk evaluation and mitigations strategy (REMS) violations.
- Issued the first 90-day decisional letter following a surveillance inspection on December 20, 2017, under [Generic Drug User Fee Act \(GDUFA\)](#) implementation.
- Issued the first Certificate of Confidentiality under the [21st Century Cures Act](#). Certificates of Confidentiality protect the privacy of participants enrolled in clinical research.
- Published the first in a series of [compounding risk alerts](#) to rapidly inform health care professionals of concerns regarding compounded drugs that present safety risks so they can more effectively protect patients from unsafe, ineffective or poor quality compounded medicines.







## CDER/Office of Compliance 2017 at a Glance

- Drug shortages: Assisted in the prevention and mitigation of drug shortages for 31 products by exercising regulatory flexibility in 55 instances.
- Bioresearch monitoring: Updated the [Sponsor Compliance Program Guidance Manual](#) for CDER's Bioresearch Monitoring program on April 19, 2017.
- Good clinical practice: Oversaw inspections for more than 130 new drug applications (NDAs) and biologics license applications (BLAs).
- Stakeholder engagement and outreach: Held nearly 150 meetings with stakeholders, including regulatory meetings with industry and listening sessions with various stakeholder associations, and presented at conferences.
- Public engagement: Held four public meetings related to compounding and supply chain security.
- Guidance documents: Issued nine final and draft guidance documents for industry related to compounded and repackaged drugs and supply chain security.
- Supply chain security outreach: As part of the [Know Your Source: Protecting Patients from Unsafe Drugs](#) program, developed a [notice to physicians](#) to educate them about the patient health risks and criminal liability associated with purchasing unapproved prescription drugs from unlicensed sources. Distributed more than 9,700 copies of this flyer to physician offices.
- Employee retention: Maintained 92 percent capacity for full-time employees, which is the highest occupancy rate of any office in CDER.



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## Director's Message

Welcome to the 2017 Annual Report for CDER Compliance in FDA's Center for Drug Evaluation and Research. Our mission is to shield patients from unsafe, ineffective and poor-quality drugs through proactive compliance strategies and risk-based enforcement actions.

We know that the American public depends on us to ensure the medications they and their family members need are effective, will not harm them and are of the highest quality. Striving to meet these high expectations drives everything that we do.

This report describes the widely different activities that CDER Compliance undertook during 2017 to accomplish our mission and meet the high expectations of the American public.

Over the past year, we have also worked to embrace the symmetries among our offices and to better align and streamline office functions. These efforts have allowed us to improve timeliness and focus on risk-based decisions and regulatory and enforcement actions, as well as to harmonize our priorities and place the spotlight on protecting patients from harmful drugs.

I am proud of the talented and dedicated professionals who serve in CDER Compliance, the work we do and the regulatory advancements we continue to make in the name of protecting public health. I look forward to even more in 2018.



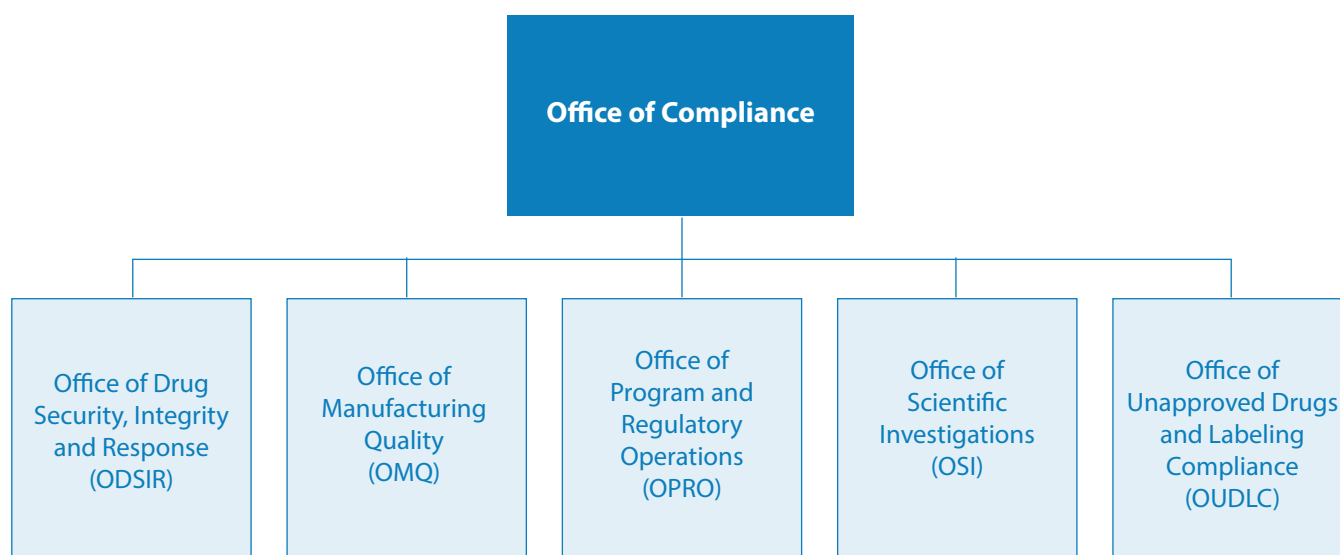
**Donald D. Ashley, J.D.**  
Director, CDER Office of Compliance

**"American patients rely on us every day to protect them from harmful drugs. Their safety remains our highest priority."**

## CDER's Office of Compliance Overview

**Mission:** To shield patients from poor quality, unsafe and ineffective drugs through proactive compliance strategies and risk-based enforcement actions.

**Vision:** To be a model of efficiency, innovation and operational excellence. Guided by law and science, we make strategic and risk-based decisions, communicate clearly with all stakeholders, foster global collaboration, promote voluntary compliance and take decisive action.



CDER Compliance is made up of five component offices that have responsibilities to protect patients throughout the lifecycle of a drug product:

- **ODSIR:** Office of Drug Security, Integrity, and Response protects the integrity of the legitimate drug supply chain. ODSIR uses a risk-based approach to minimize consumer exposure to dangerous products marketed outside the legitimate supply chain.
- **OMQ:** Office of Manufacturing Quality works to ensure drugs marketed to U.S. consumers are high quality and comply with current good manufacturing practice (CGMP) requirements by reviewing manufacturing facility inspection findings to determine if drug products consistently meet CGMPs. OMQ develops and implements compliance and enforcement actions to ensure compliance with federal law.
- **OPRO:** Office of Program and Regulatory Operations leads and manages operational infrastructure for CDER Compliance relating to project and process management. OPRO also manages the [electronic drug registration and listing database \(eDRLS\)](#) and works to ensure that information in the database is up to date and accurate.
- **OSI:** Office of Scientific Investigations helps ensure that CDER-regulated drugs, biologics and biosimilars have reliable evidence of safety and effectiveness and meet post-market safety requirements. OSI also protects

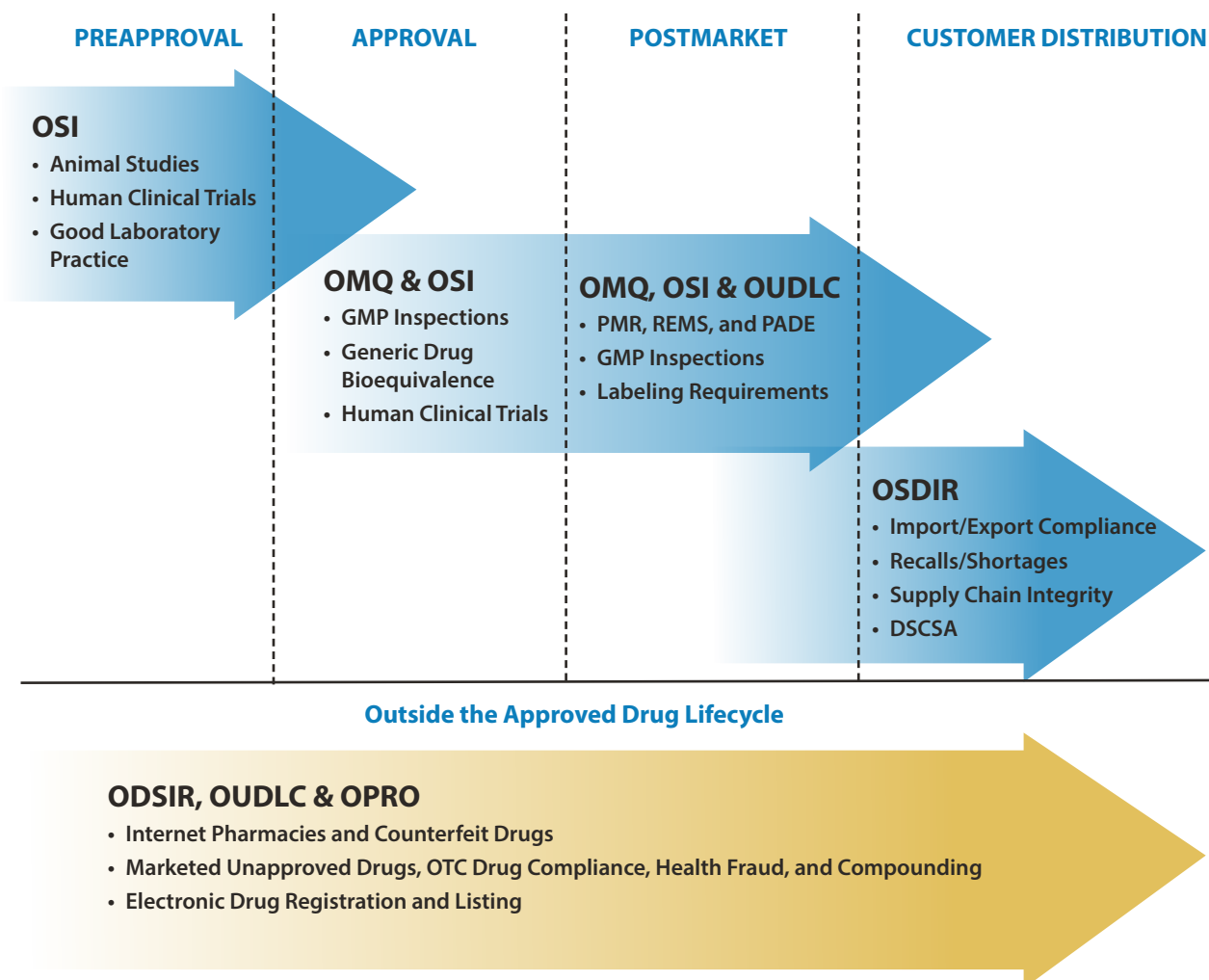


the rights, safety and welfare of human subjects in clinical trials. In collaboration with the Office of Study Integrity and Surveillance, OSI administers FDA's [bioresearch monitoring \(BIMO\) compliance programs](#).

- **OU DLC:** Office of Unapproved Drugs and Labeling Compliance develops policies and compliance strategies to aid in ensuring that over-the-counter and prescription drugs are properly labeled and meet drug approval requirements. OUDLC engages in strategic, risk-based, compliance activities to minimize consumer exposure to unsafe, fraudulent and compounded drugs.

CDER Compliance's mission is to shield patients from poor quality, unsafe and ineffective drugs through compliance strategies and risk-based enforcement actions.

## Responsibility Throughout Lifecycle



10722 14-311-  
72009Cb =pH[H<sup>+</sup>][OH<sup>-</sup>]

Analysis: Complete.  
 Position: #120498 05  
 Offset: 64005 980 011B  
 Current status: Online

Cb =pH[H <sup>+</sup> ]	[OH <sup>-</sup> ]	Alpha	Beta
7.403.98E-08	2.51E-07	0.201	0.201
7.602.51E-08	3.98E-07	0.285	0.285
8.001.00E-08	1.00E-06	0.500	0.500
8.403.98E-09	2.51E-06	0.715	0.715
8.801.58E-09	6.31E-06	0.863	0.863
9.001.00E-09	1.00E-05	0.909	0.909

## Key Compliance Initiatives

We are dedicated to protecting Americans from harmful drug products and worked on many priority initiatives in 2017 to fulfill this mission. These are some of the highlights:

### Implementing the compounding provisions of the FD&C Act and conducting oversight to protect public health

Advancing the FDA's compounding program is a high priority for the agency. As part of this program, we:

- diligently work to implement the compounding provisions of the FD&C Act, as amended by the Drug Quality and Security Act (DQSA) in 2013;
- conduct oversight through inspections;
- take regulatory and enforcement actions, when appropriate, to protect public safety;
- engage with stakeholder organizations to hear their views about FDA's policies; and
- partner with states to collaborate on our shared public health goals.

We kicked off 2017 by issuing a [progress report](#) describing our policy development, oversight and stakeholder outreach initiatives, as well as our priorities going forward. Since then, we have made significant progress implementing the compounding provisions of federal law, engaging in robust oversight to identify and address safety and quality concerns and collaborating with stakeholders. Although FDA has seen improved compliance with certain requirements of federal law, we continue to see serious adverse events and product quality defects related to sterile and non-sterile compounded drugs, as well as other egregious conditions and practices that put patients at risk.

In 2017, we embarked on several new initiatives to promote compliance and share information to benefit public health. For example, we implemented an important new communication tool called a [compounding risk alert](#) to inform prescribers and other practitioners of safety risks associated with certain compounded drugs or practices. These alerts inform health care professionals about adverse event reports related to compounded drugs, so

practitioners can more effectively protect patients from unsafe, ineffective and poor quality compounded medicines. These alerts are particularly important given the many serious patient illnesses and deaths linked to poor quality compounded drugs.

**Examples of oversight activities that FDA conducted in 2017 include:**

OVERSIGHT ACTIVITIES	CY 2017
Inspections of compounders	143
Warning letters advising compounders of significant violations of federal law	58
Letters referring inspectional findings to state regulatory agencies	49
Recall events overseen by FDA involving compounded drugs	38
Civil enforcement actions in collaboration with the Department of Justice	2
Voluntary temporary or permanent cessations of operations by compounders	14

To further our collaboration and engagement with our state government partners, we held our sixth [annual inter-governmental meeting](#) in September 2017 to discuss compounding oversight and DQSA implementation, and to identify opportunities to better protect public health by strengthening oversight of compounders through federal-state collaboration. We also provided training to state pharmacy compliance officers regarding FDA inspections of compounding facilities.

We also published a document, [“Information for Outsourcing Facilities,”](#) to assist compounders in locating provisions of the FD&C Act and FDA policy and procedures relevant to the operations of outsourcing facilities, and in deciding whether to register with FDA as an outsourcing facility. In this document, we advised that FDA would entertain, as resources permit, requests from outsourcing facilities and compounders to meet with the agency prior to registering as an outsourcing facility. We also spoke at industry conferences to further our engagement and collaboration with outsourcing facilities and health care professionals.

As part of our work to implement the FD&C Act, we issued two [guidance documents](#) (one final and one revised draft). The final guidance addresses repackaging of certain human drug products by pharmacies and outsourcing facilities, and the revised draft addresses mixing, diluting and repackaging of biological products. We also issued a Federal Register notice establishing a public docket for the public to submit additional information about drug products that present demonstrable difficulties for compounding.

Additionally, we held two [Pharmacy Compounding Advisory Committee](#) meetings. The first meeting sought advice on bulk drug substances that stakeholders have nominated to be used in compounding. The second meeting sought advice on drug products that stakeholders nominated for inclusion on the list of drugs that have been withdrawn and removed from the market for safety or effectiveness reasons.

## Implementing the Drug Supply Chain Security Act (DSCSA)

The [DSCSA](#) outlines critical steps to build an electronic, interoperable system by 2023 to trace certain prescription drug products distributed in the United States. The new system will enhance FDA’s ability to protect consumers from

exposure to drugs that may be counterfeit, stolen, intentionally adulterated or otherwise harmful through improved detection and removal of such products from the drug supply chain. We have been working with supply chain stakeholders to implement the law since enactment in 2013.

In 2017, to avoid disruption in the supply chain, we provided an additional year to manufacturers to serialize products by encoding a unique [product identifier](#) to prescription drug packages in a 2-dimensional barcode. The product identifier includes the drug's National Drug Code (NDC), serial number, lot number and expiration date. Manufacturers have until November 2018 to serialize their products. We issued [draft guidance](#) that explained a product without a product identifier would be grandfathered if there were accompanying documentation that it was packaged by a manufacturer before November 27, 2018.

We also announced our intent to establish a [pilot project program](#) to assist in the development of the electronic, interoperable system that will identify and trace certain prescription drugs distributed within the United States. We intend to initiate the program in 2018.

We held the first two [public meetings](#) in a series to further engage stakeholders on strategies for an enhanced drug distribution security under the DSCSA. These meetings provided supply chain stakeholders an opportunity to discuss strategies and issues. We continued our outreach and engagement with stakeholders by holding one stakeholder listening session and meeting with a variety of stakeholder groups, as well as presenting at conferences to further engage with stakeholders.

## FDA issues warning letters to companies selling illegal cancer treatments

We worked with other FDA centers to issue 14 [warning letters](#) targeting U.S.-based companies illegally selling more than 65 products that fraudulently claim to prevent, diagnose, treat or cure cancer. The products were marketed and sold without FDA approval and in violation of the FD&C Act, most commonly on websites and social media platforms.

As part of this announcement, we conducted media interviews and several of the major news outlets helped us warn consumers of the deceptive claims made by the marketers of these products. We continue to urge patients to beware and protect themselves as these (and other) products could cause harm to patients who use them. Although many of these companies have stopped selling the products or making fraudulent claims, numerous unsafe and unapproved products continue to be sold directly to consumers due in part to the ease with which companies can move their marketing operations to new websites.

We continue to monitor the internet and retailers for these products and will continue to take action against companies promoting and selling unproven treatments to minimize the potential dangers to consumers.

## Supporting FDA's hurricane relief efforts

We supported FDA's hurricane relief efforts in 2017, and much of this work has continued in 2018. Our top priorities were ensuring the safety of our employees that live in areas devastated by the hurricanes and working with the pharmaceutical manufacturing facilities in Florida and especially Puerto Rico. Specifically, we:

- worked with Drug Shortage Staff to allow for the temporary import of [sterile saline solutions](#) from Baxter International facilities in Ireland, Australia, Mexico, Canada and Brazil; and from B. Braun in Germany after Hurricane Maria disrupted Baxter's IV fluid production facilities in Puerto Rico, reducing the availability of saline in the United States;



- prioritized impacted facilities to determine the order in which FDA investigators would conduct necessary inspections;
- supported 30 CDER Compliance employees who are also members of the Public Health Service Commissioned Corps as they deployed to support the Department of Health and Human Services relief efforts; and
- clarified [supply chain requirements under the DSCSA](#) due to the public health emergency declaration following the hurricanes to ensure that U.S patients received needed medications during the relief efforts.

## CDER Compliance's incident management team responds rapidly to public health issues

We work to quickly investigate and respond to emergencies impacting public health. This year, we:

- Warned consumers not to use homeopathic teething products – Our work on the homeopathic teething products began in 2016; by January 2017, FDA testing had found the products contained [elevated levels of belladonna](#). We worked with a cross-agency team to remind consumers not to use these products due to the toxicity risk.
- Alerted patients and health care professionals to a Burkholderia cepacia outbreak – We worked with a cross-agency team on the [2017 Burkholderia cepacia outbreak](#) involving products made by PharmaTech LLC. As part of this second multi-state outbreak, FDA testing identified B. cepacia in one lot of Rugby Diocto (docusate sodium) oral liquid, which was manufactured by PharmaTech. We worked efficiently to remind consumers and health care professionals not to use any liquid products manufactured by PharmaTech due to the risk of contamination.

## FDA proposes a risk-based enforcement priorities approach to protect consumers from potentially harmful, unproven homeopathic drugs

We worked with CDER's Office of Regulatory Policy to develop a proposal for a [new, risk-based enforcement approach](#) to drug products labeled as homeopathic.



[FDA homeopathic product label graphic](#) that represents the many popular but untested, unproven and potentially harmful OTC homeopathic products currently on the market.

The proposed approach prioritizes enforcement and regulatory actions involving unapproved drug products labeled as homeopathic that have the greatest potential to cause risk to patients. Under this approach, many homeopathic products will likely fall outside the risk-based categories described in the new draft guidance and will remain available to consumers. We intend to focus our enforcement authorities on the following kinds of products:

- products with reported safety concerns;
- products that contain or claim to contain ingredients associated with potentially significant safety concerns;

- products for routes of administration other than oral and topical;
- products intended to be used for the prevention or treatment of serious and/or life-threatening diseases and conditions;
- products for vulnerable populations; and
- products that do not meet standards of quality, strength or purity as required under the law.

## Warning consumers about SARMs, steroids and steroid-like substances in body-building products

We alerted consumers to unscrupulous companies marketing body-building products with potentially dangerous ingredients. These products are not FDA-approved and are associated with serious safety concerns, including potential to increase the risk of heart attack or stroke and life-threatening reactions like liver damage.

We issued three warning letters to companies distributing products containing selective androgen receptor modulators, or [SARMs](#).



Three body-building products illegally marked with potentially dangerous ingredients.

We also issued three warning letters to companies illegally marketing products labeled to contain [steroid and steroid-like substances](#) and promoted to increase muscle mass and strength. From July 1, 2009, to December 31, 2016, we received [35 reports of serious liver injury](#) associated with body-building products that are labeled or suspected to contain steroids or steroid alternatives. Other known adverse health consequences from these types of products include kidney injury, increased risk of heart attack and stroke and shrinkage of the testes and male infertility.

We advised consumers to stop using these body-building products immediately and consult a health care professional if they experience any adverse reactions that may be associated with their use.

Since these warning letters issued, all six companies have stopped selling the products cited in the warning letters.

## Warning companies marketing unproven products, derived from marijuana, that claim to treat or cure cancer

In a collaborative effort we worked with other offices in FDA to issue [warning letters](#) to four companies illegally marketing products online that claim to prevent, diagnose, treat or cure cancer without evidence to support these outcomes. The warning letters cited more than 25 different products, being marketed with unsubstantiated claims, spanning multiple websites, online stores and social media websites. All the products allegedly contained cannabidiol (CBD), a component of the [marijuana](#) plant.

## Targeting illegally marketed opioids and other drugs sold online in global operation

We once again participated in [Operation Pangea](#), targeting illegally marketed opioids and other products, along with the websites that sell them. We collaborated with FDA's Office of Criminal Investigations (OCI) and issued 13 [warning letters](#) to the operators of 401 websites, while OCI seized nearly 100 website domain names. These websites illegally sold potentially dangerous, unapproved versions of prescription medicines including opioids, antibiotics and injectable epinephrine products to American consumers.

Patients who buy prescription medicines from [illegal online pharmacies](#) may be putting their health at risk because the products, while being passed off as authentic, may be counterfeit, contaminated, expired or otherwise unsafe. Rogue online pharmacies are often run by sophisticated criminal networks that knowingly and unlawfully distribute drugs illegally, including counterfeit medicines and controlled substances. Consumers use these websites believing that they are buying safe and effective medications, but they are being deceived and put at risk by individuals who put financial gains above patient safety. Further, the easy and illegal availability of these controlled substances fuels the misuse and abuse of opioids.

## Working to ensure accuracy of the drug registration and listing database

Many groups and programs across the agency and in industry rely on the accuracy and completeness of the data submitted by companies as part of the drug establishment registration and listing regulatory requirements. We monitor the integrity of this data through its registration and listing compliance program and work with companies to make the required revisions when necessary.

In 2017, we worked to implement the new requirements under [Part 207 of the Code of Federal Regulations](#) (21 CFR 207), which improves management of [drug establishment registration and drug listing](#). As part of the new requirements, companies must annually update or certify that there are no changes to their drugs listings. This applies to drug listings that were not initially listed or updated during the current calendar year.

To help guide stakeholders, we conducted outreach, which included working with the CDER Small Business and Industry Assistance (SBIA) program to hold an all-day [public workshop and webinar](#), as well as participating in several industry meetings.

## Enhancing the agency's BIMO program

We collaborate with the Office of Study Integrity and Surveillance (OSIS) and the Office of Regulatory Affairs (ORA) to ensure the protection of subjects involved in clinical and non-clinical research for FDA-regulated products. Additionally, we work directly with ORA's Office of Bioresearch Monitoring Operations (OBIMO) to ensure the

quality and integrity of data in clinical and non-clinical studies that support the research and marketing applications submitted for review. Specifically, we:

- protect human research subjects' rights, safety and welfare;
- ensure quality, reliability and integrity of research data; and
- ensure that FDA-regulated research is conducted in compliance with applicable federal law.

In May 2017, OBIMO was formally launched, creating the only agency-wide regulatory program that involves a dedicated workforce supporting the entire agency. We played a significant role in establishing the infrastructure needed to support and guide the BIMO program, defining success metrics, developing common practices and communications across all the BIMO compliance programs and redefining surveillance activities for most efficient utilization of inspectional resources.

We led activities such as establishing a BIMO Governance Board, implementing best practices and harmonizing center processes. We also led the development and execution of training on key elements of safety, human subject protection and data reliability available to the entire BIMO workforce.

The postmarketing adverse drug experience (PADE) and risk evaluation and mitigation strategies (REMS) global inspections programs also were migrated into the BIMO regulatory program to enable more effective oversight of the products regulated and help fulfill the agency's obligation to protect American patients from unsafe drugs.

This transition enhances the agency's mission by providing clarity in roles and responsibilities, strengthening the workforce, minimizing resources and improving cross-agency communication and collaboration.

## **Collaborating with Office of Regulatory Affairs and CDER's Office of Pharmaceutical Quality to strengthen FDA's inspection and oversight of drug manufacturing**

While working on [Program Alignment](#), CDER and ORA identified an opportunity to further enhance FDA's operational capacity by eliminating overlapping efforts among CDER and ORA offices. This [concept of operations](#) agreement, or ConOps, which was issued on June 6, 2017, outlines responsibilities and workflows that help streamline human drug facility evaluations, inspections and communication.

ConOps enables CDER and ORA to more effectively manage the growing complexity of the pharmaceutical landscape. ConOps supports Generic Drug User Fee Amendments II (GDUFA II) FY19 commitment to communicate final inspection classifications that do not negatively impact approvability of any pending application within 90 days of the end of the inspection. It also creates a 90-day decisional letter for surveillance inspection outcomes and six-month goal date for issuing warning letters.

We issued the first 90-day decisional letter on December 20, 2017. Our goal is to issue 90 percent of these decisional letters in under 90 days from inspection beginning in October 2018.

ConOps reduces the chance that inspectional issues will cause approval delays and allows us to communicate more quickly when manufacturing problems are identified.





## Proactively Promoting Compliance

We believe that the best way to minimize the detrimental impact of potentially harmful drugs is to prevent violations of FDA laws before they occur. Therefore, we focus on proactively promoting compliance through clear communication and collaboration with all stakeholders. We help facilitate understanding and knowledge of federal laws with a shared goal of achieving voluntary compliance.

In 2017, we worked to enhance our outreach efforts on numerous program areas to proactively promote compliance across all sectors of the pharmaceutical industry. In addition to warning letters and other regulatory actions that we take to alert companies to violations, we engage industry and other stakeholders in a variety of ways, including authored articles in trade publications, conference presentations, listening sessions and workshops.

In this global pharmaceutical environment, collaboration on a global scale is vital to protecting consumers from harmful drug products. Whether protecting patients from potentially counterfeit drugs sold online or collaborating with other countries during an inspection, this work is critical to keeping the U.S. drug supply chain safe.

We will continue to seek opportunities to collaborate and combine our efforts with industry and other stakeholders and seek to ensure that patients have access to safe, effective and quality drug products.

### Improving communication with manufacturing facilities

CDER Compliance has worked to more quickly communicate inspectional outcomes to manufacturing facilities that are violating CGMP requirements over the past three years. The goal is to inform manufacturers of the significant CGMP violations for them to take the appropriate corrective actions and improve their overall compliance with CGMP

requirements. In turn, this will improve the overall quality of drug products they produce. When compared to 2015, there has been a 55 percent improvement in the time between a final inspection report to the issuance of a warning letter.

2015	2016	2017
11 months on average	9 months on average	5 months on average

## International collaboration: An important component for promoting compliance in the global market

### FDA and European Union (EU) agree to a new framework for pharmaceutical inspections

The [Mutual Recognition Agreement](#) allows FDA and EU drug investigators to rely on information from CGMP drug inspections conducted within each other's borders.

In 2012, Congress passed the Food and Drug Administration Safety and Innovation Act (FDASIA), which gave the FDA authority to enter into agreements to recognize drug inspections conducted by foreign regulatory authorities if the FDA determined those authorities were capable of conducting inspections that met U.S. requirements. Since May 2014, the FDA and the EU have been collaborating to evaluate the way they each inspect drug manufacturers and assessing the risk and benefits of mutual recognition of drug inspections.

In October 2017, FDA [announced](#) eight countries with capability assessments as part of the “Mutual Reliance Initiative” – Austria, Croatia, France, Italy, Malta, Spain, Sweden and the United Kingdom. We assisted in these assessments and continues to collaborate with other CDER offices and FDA centers on additional assessments.

### Leading international efforts to create a Supply Chain Security Toolkit for Medical Products

Protecting the integrity of the medical product supply chain is complex and requires a global approach. We led FDA's collaboration with Asia Pacific Economic Cooperation (APEC) economies to create a [Supply Chain Security Toolkit for Medical Products in 2017](#), which maximizes available global resources, delivers quality trainings and best practices, and secures the global supply chain for medical products. The toolkit covers the entire supply chain and lifecycle of medical products, from raw materials to use by patients. It focuses on developing — and implementing through training programs — processes, procedures and tools directed at enhancing global medical product quality and supply chain security.

Comprehensive product quality and [supply chain security](#) requires a multi-layer approach that includes prevention, detection and response strategies and actions. The toolkit is a comprehensive resource that addresses areas of vulnerability in the medical product supply chain and contains recommended best practices and tools to prevent and detect substandard and falsified medical products before they reach consumers. It also provides tools to efficiently and effectively respond to incidents involving substandard and falsified medical products.

As the medical products industry has become more globalized and specialized, countries must increasingly rely on the global marketplace to provide the medical products needed to keep consumers healthy and ensure that access to legitimate products is not disrupted. Industry stakeholders and regulators from around the globe use the toolkit to adopt best practices, for training purposes and to strengthen laws to protect consumers from unsafe and substandard drug products.



Asia Pacific Economic Cooperation ([APEC Supply Chain Security Toolkit](#)) front interface.

## Japan joined FDA/European Medicines Agency (EMA) in Good Clinical Practice (GCP) Initiative

Pharmaceuticals and Medical Devices Agency (PMDA) Japan joined the FDA and EMA CGP initiative in June 2017, as an observer, to assess opportunities for increased information sharing and collaboration.

The GCP Initiative was launched as a pilot in September 2009 under the confidentiality arrangements established between the European Commission, EMA and FDA. Through this initiative, the countries share information on inspections and GCP-related documents of common interest, as well as conduct collaborative inspections.

After the 18-month pilot phase ended in 2011, EMA and FDA continued the GCP collaboration. The communication among the two agencies facilitated improvements in GCP-inspection coverage and decision-making processes. As the result, EMA and FDA continue conducting periodic information exchanges on GCP-related information, collaborate on GCP inspections and share information on the interpretation of GCP.

## Collaborating with the Medicines and Healthcare Products Regulatory Agency (MHRA) on GCP/ BIMO initiative

In 2017, FDA continued to collaborate with the MHRA under an existing confidentiality agreement with regards to GCP/BIMO inspections. This collaboration includes discussing common applications, inspection results and trends and issues seen within the industry.

### Engagement by the numbers in CY 2017:

Types of Engagements	2017
Public meetings	4
Regulatory meetings with industry	35
Listening sessions	8
Conference presentations	85
Inter-governmental/50-state meeting	1
External trainings	3
Webinars	2

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We work with many stakeholders and industry to help facilitate understanding and knowledge of federal laws and FDA regulations with a shared goal of achieving voluntary compliance.

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## Compliance Actions by the Numbers

- Issued 66 [immediate public notifications](#) regarding fraudulent health products in CY 2017.
- Issued 30 [online advisory letters](#) to companies making fraudulent serious disease claims in CY 2017.
- Issued four [compounding risks alerts](#) in CY 2017.

Number of drug-specific warning letters (except advertising violations) in CY 2017	
ODSIR	14
OMQ	76
OPRO	4
OSI	8
OULDLC	75
<b>Total</b>	<b>177</b>

Number of drug-related CGMP warning letters that included data integrity violations in CY 2017	
Total number of GMP WLs	Number of CGMP WLs that included data integrity violations
76	32

Number of drug-related recall events overseen by CDER Compliance in CY 2017	
Class I	39
Class II	187
Class III	117

Number of recalled drug products overseen by CDER Compliance in CY 2017	
Class I	66
Class II	883
Class III	179

Six Injunctions Obtained in CY 2017	
June 15	<a href="#">Sonar Products ordered to cease operations, Stratus Pharmaceuticals ordered to cease distributing unapproved drugs</a>
July 6	<a href="#">Federal judge enters consent decree against Alabama compounder Medistat</a>
July 27	<a href="#">District court enters permanent injunction against Tennessee company and its CEO to stop distribution of unapproved and misbranded drugs</a>
August 4	<a href="#">Federal judge enters consent decree against outsourcing facility Isomeric Pharmacy Solutions</a>
September 22	<a href="#">Criminal and civil actions filed against Aegerion Pharmaceuticals Inc.</a>
September 26	<a href="#">Federal judge orders Flawless Beauty to stop distributing unapproved drugs, recall certain products</a>



## Proactively keeping dangerous drugs from entering the U.S. supply chain

We collaborate with other offices in FDA to issue import alerts to inform FDA staff and industry that we have evidence of a violation justifying the detention of a product without physical examination at our borders. Violations include those related to the product, manufacturer or shipper, as well as other issues. Import alerts are a critical compliance tool because they:

- prevent potentially violative products from being distributed within the United States;
- free up agency resources to examine other shipments; and
- help provide consistency for import entry review at ports.

Highlights of our work on import alerts in CY 2017 include:

- Adding 45 facilities to [import alert 66-40](#), which lists manufacturing facilities that, based on an FDA inspection, are not operating in conformity with CGMP requirements;
- Adding or updating 57 companies to [import alert 66-41](#), which lists companies and products for which we have sufficient evidence to demonstrate that a product appears to be an unapproved new drug; and
- Adding 21 facilities to [import alert 99-32](#), which lists companies and their products that appear to be adulterated because the companies have refused to permit FDA to inspect the facility.



## Looking Ahead

We expect 2018 to be another busy year. Throughout the year, we will work to communicate and engage with industry and stakeholders to increase voluntary compliance to help shield patients from all types of unsafe, ineffective and poor-quality drugs. When companies fail to comply with the law, we will pursue effective and risk-based regulatory actions that have the biggest impact on public health. For example, we will focus on three key areas: enforcement related to unlawful manufacture and distribution of opioids, implementing the FDA's Compounding Policy Priorities Plan and continuing to enhance supply chain security.

### Helping address the opioid crisis

We will conduct targeted enforcement efforts to help address opioid overdose related deaths. In January 2018, we issued two [warning letters](#) to marketers of homeopathic drugs that illegally claimed their products helped in the treatment of opioid addiction and withdrawal. Health fraud scams like these can pose serious health risks. These products have not been demonstrated to be safe or effective and may keep some patients from seeking appropriate, FDA-approved therapies. Throughout 2018, we will continue to monitor the marketplace for these and other fraudulent products. We will work with FDA investigators to conduct targeted inspections aimed at ensuring opioids are safe, effective and labeled in accordance with FDA requirements, as well as expand the [REMS](#) inspection programs.

### Commissioner announces 2018 Compounding Policy Priorities Plan

Since DQSA was enacted in 2013, we have worked aggressively to implement this new law, and this work will continue throughout 2018. FDA recently issued a [2018 Compounding Policy Priorities Plan](#), which outlines how the agency

will implement certain key aspects of the DQSA and other provisions of the law relevant to compounders. The 2018 Compounding Policy Priorities Plan details how FDA will:

- address manufacturing standards for outsourcing facilities;
- regulate compounding from bulk drug substances;
- restrict compounding of drugs that are essentially copies of FDA-approved drugs;
- solidify FDA's partnership with state regulatory authorities; and
- provide guidance on other activities that compounders undertake.

As we meet our obligations under DQSA, we will balance the need to preserve access to appropriately compounded drugs for patients who have a medical need for these products with the need to help protect patients from poor quality compounded drugs that could cause harm.

## **DSCSA implementation continues to be a priority in 2018**

We also will continue our work to implement DSCSA and the 2023 deadline to implement a fully electronic, interoperable, package-level tracing to enhance the drug distribution system to enable trading partners to trace certain prescription drugs as they move within the U.S. drug supply chain. We envision that this new electronic system should be designed to provide increased public health benefits by creating a tighter, closed system that will prevent the introduction of illegitimate products, better detect suspect and illegitimate products and enable us and stakeholders to rapidly respond when such products are found in the drug supply chain.

Our stakeholder collaboration will focus on building a clear path forward on what the system will do, what the regulatory and legal requirements are, how to operationalize the system and how to ensure that it is agile enough to adapt to future changes in technology and drug distribution in the United States to best protect patients from exposure to drugs that are potentially harmful.

We are also working to develop new standards for licensure of wholesale distributors and third-party logistic providers (3PLs) as required in DSCSA to improve oversight of the supply chain, and we intend to publish proposed regulations in 2018.



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